

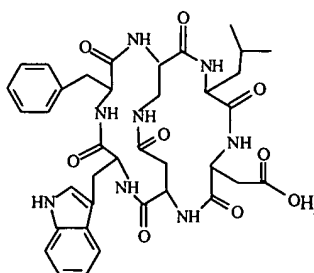
**Amendments to the Claims :**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (Original) Process for preparing bicyclic peptide compounds of formula (I)

Cyclo(Asp(OH)Asp-Trp-Phe-Dpr-Leu)



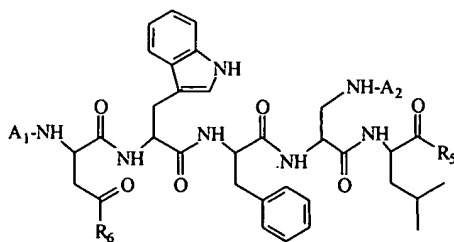
(I)

comprising the following steps:

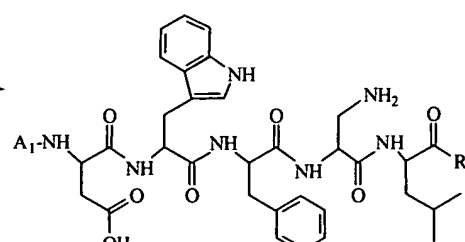
- 1) deprotection of the linear pentapeptide of formula (II) in the presence of a solvent to give the compound of formula (III):

$A_1$ -Asp( $R_6$ )-Trp-Phe-Dpr( $A_2$ )-Leu- $R_5$

$A_1$ -Asp(OH)-Trp-Phe-Dpr(H)-Leu- $R_5$



(II)

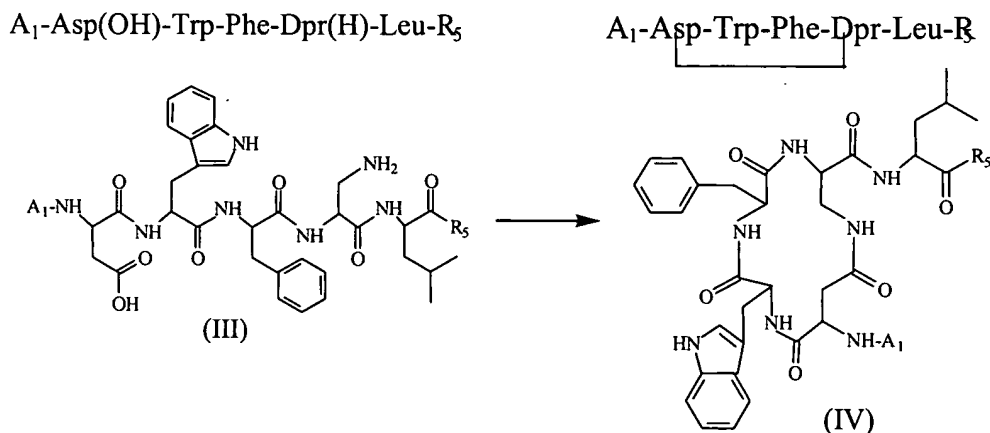


(III)

wherein  $A_1$  and  $A_2$  are two nitrogen protecting groups different from each other, and  $R_5$  and  $R_6$ , different from each other, are chosen from benzyloxy and lower alkyloxy groups in which the alkyl part comprises a linear or branched C1-C4 group;

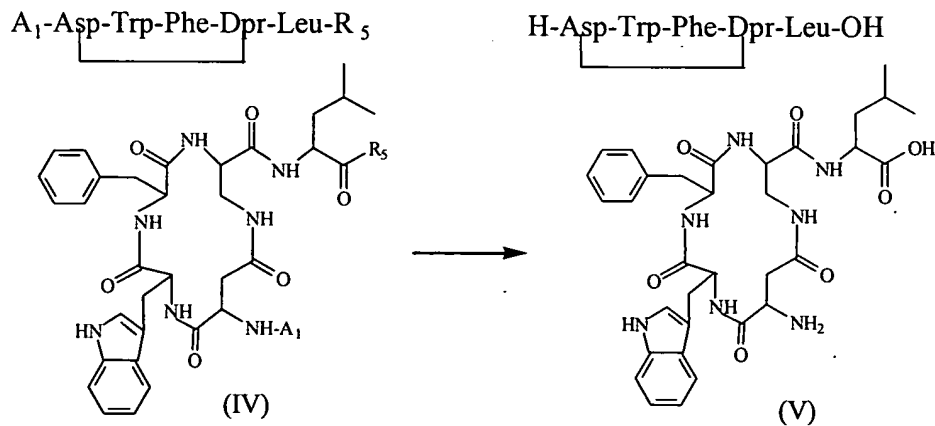
- 2) intramolecular cyclisation of the compound of formula (III) coming from step 1) in the

presence of a solvent and of a suitable coupling agent to give the compound of formula (IV)



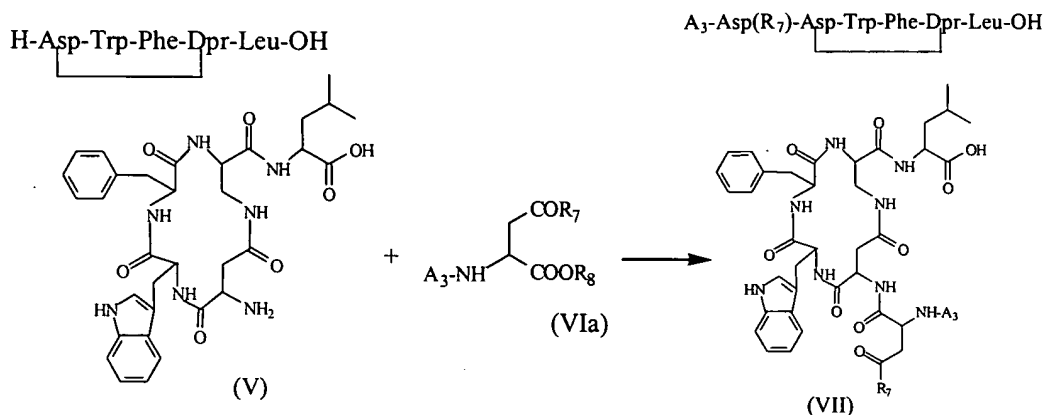
wherein  $R_5$  is as defined above;

3) deprotection of the compound of formula (IV) coming from step 2) in the presence of a solvent to give the compound of formula (V)



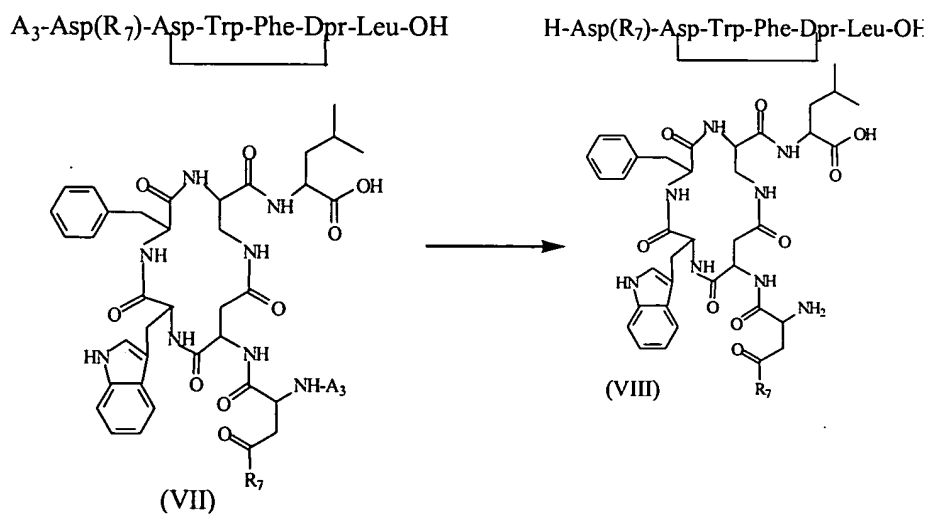
wherein  $R_5$  is as defined above;

4) coupling between the compound of formula (V) coming from step 3) and a protected amino-acid of formula (VIa) in the presence of a solvent, to give compounds of formula (VII)



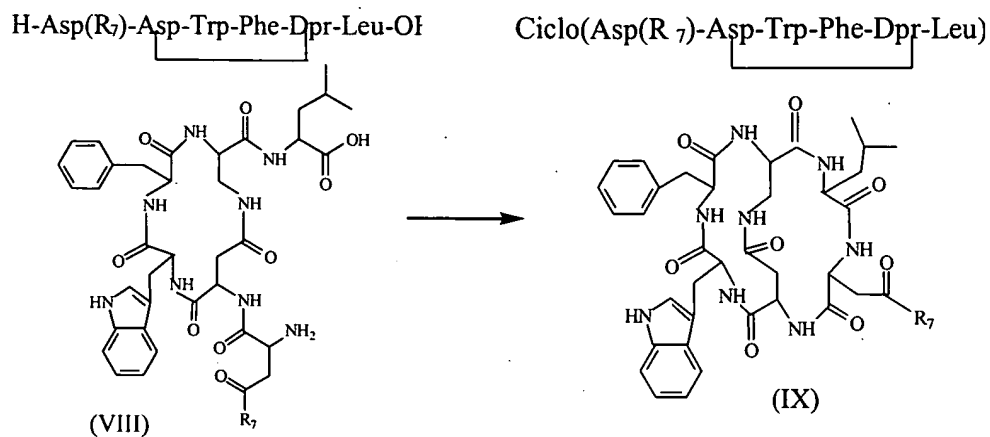
wherein A<sub>3</sub> is a nitrogen protecting group; R<sub>7</sub> is chosen from benzyloxy and lower alkyloxy groups, in which the alkyl part comprises a linear or branched C1-C4 group; R<sub>8</sub> is a residual group deriving from an activation procedure on the carboxyl group;

5) deprotection of the compound of formula (VII) coming from step 4) in the presence of a solvent to give a compound of formula (VIII)



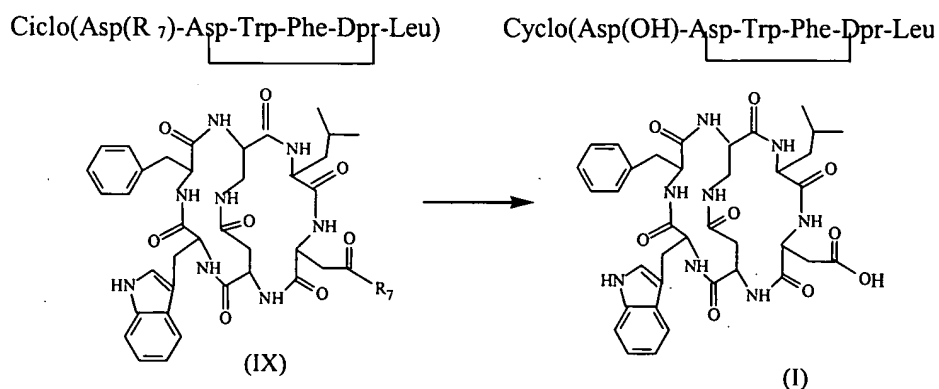
wherein R<sub>7</sub> is as defined above;

6) intramolecular cyclisation, in the presence of a solvent and of a suitable coupling agent, of the compound of formula (VIII) coming from step 5) to give a bicyclic compound of formula (IX)



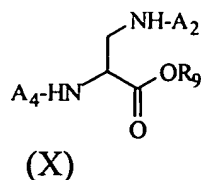
wherein  $R_7$  is as defined above;

7) deprotection of the bicyclic compound of formula (IX) coming from step 6) in the presence of a solvent, to obtain the compound of formula (I)



wherein  $R_7$  is as defined above.

2. (Currently amended) The process according to claim 1, wherein the linear peptides of formula (II) are obtained by means of a sequential coupling strategy of suitable amino acids starting from a derivative of the amino acid Dpr of formula (X), protected on nitrogen and prepared separately or generated *in situ*



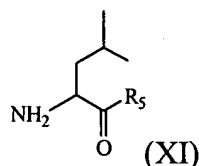
wherein

$A_2$  and  $A_4$ , different from each other, are nitrogen protecting groups;

$R_9$  is a residual group deriving from an activation procedure, preferably chosen from the group consisting of benzyloxycarbonyl, alkoxy carbonyl comprising a linear or branched C1-C4 group in the alkyl part, and succinimidyl;

according to the following steps:

- reaction of the derivative of formula (X) above reported in the presence of a solvent with a Leu ester of formula (XI)



wherein  $R_5$  is defined as in claim 1, to obtain the dipeptide  $A_4$ -Dpr( $A_2$ )-Leu- $R_5$ ,

- deprotection of the dipeptide  $A_4$ -Dpr( $A_2$ )-Leu- $R_5$ , to obtain the monodeprotected dipeptide H-Dpr( $A_2$ )-Leu- $R_5$ ;
- coupling the monodeprotected dipeptide H-Dpr( $A_2$ )-Leu- $R_5$  with the activated ester of the subsequent amino acid Phe and then successively with Trp and Asp, until the compounds of formula (II) are obtained.

3. (Currently amended) The process ~~Process~~ according to claim ~~claims 1 and 2~~, wherein the linear peptides of formula (II) are obtained by means of a synthesis strategy comprising the following steps:

- coupling of the monodeprotected dipeptide H-Dpr( $A_2$ )-Leu- $R_5$ , obtained as described in claim 2, with an activated derivative of the dipeptide of the following formula (XII)

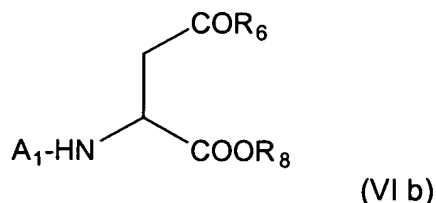


(XII)

wherein  $A_2$  and  $A_5$ , different from each other, are nitrogen protecting groups, prepared separately or generated *in situ* by coupling an activated ester of a Trp protected on nitrogen prepared separately or generated *in situ*, with a Phe ester and subsequent hydrolysis of the ester group, to obtain the tetrapeptide  $A_5$ -Trp-Phe-Dpr( $A_2$ )-Leu- $R_5$ ;

- suitable deprotection of the tetrapeptide  $A_5$ -Trp-Phe-Dpr( $A_2$ )-Leu- $R_5$  from the group attached to the nitrogen of Trp;

- coupling of the deprotected tetrapeptide with a compound of formula (VI b)



wherein  $\text{A}_1$ ,  $\text{R}_6$  and  $\text{R}_8$  are defined as in claim 1.

4. (Currently amended) The process ~~Process~~ according to claim 2 ~~claims 1-3~~, wherein the linear peptides of formula (II) are obtained by means of a synthesis strategy of the 3+2 type that involves coupling the tripeptide  $\text{A}_1\text{-Asp}(\text{R}_6)\text{-Trp-Phe-OH}$ , obtained by removing the nitrogen protecting group from the compounds of formula (XII) above reported, subsequent coupling with a compound of formula (VIb) above reported and then further coupling with the monodeprotected dipeptide  $\text{H-Dpr}(\text{A}_2)\text{-Leu-R}_5$  prepared as described in claim 2.

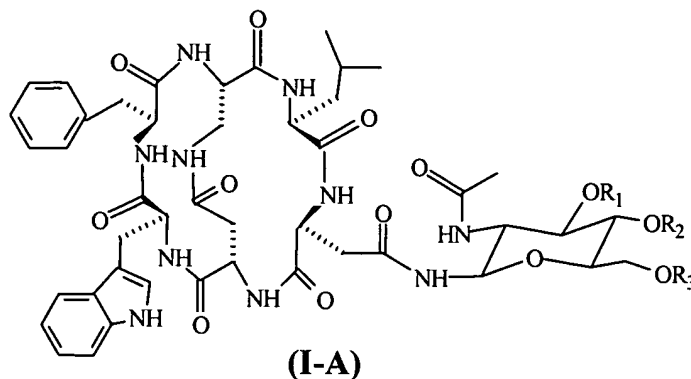
5. (Currently amended) The process ~~Process~~ according to claim 1, wherein said nitrogen protecting groups are selected from the group consisting of benzyloxycarbonyl and alkoxy carbonyls in which the alkyl part comprises a linear or branched C1-C4 group.

6. (Currently amended) The process ~~Process~~ according to claim 5, wherein said nitrogen protecting groups are selected from t-butoxycarbonyl and benzyloxycarbonyl.

7. (Currently amended) The process ~~Process~~ according to claim 1, wherein said  $\text{R}_8$  group is selected from the group consisting of benzyloxycarbonyl, alkyloxycarbonyl comprising a linear or branched C1-C4 group in the alkyl part, succinimidyl, benzotriazole possibly substituted by a halogen and azabenzotriazole.

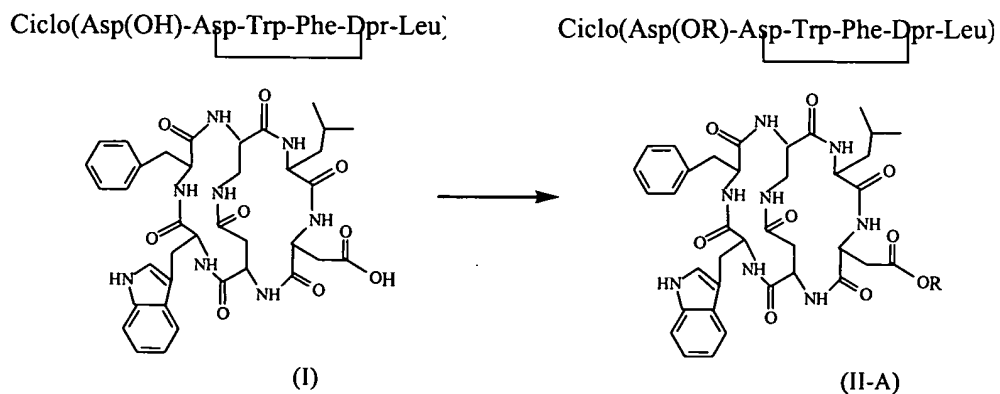
8. (Currently amended) The process ~~Process~~ according to claim 1 ~~claims 1-7~~, wherein said linear or branched C1-C4 group is selected from the group consisting of methyl, ethyl, propyl, butyl, isopropyl and t-butyl.

9. (Currently amended) A process ~~Process~~ for preparing a bicyclic glycopeptide compound of formula (I-A)



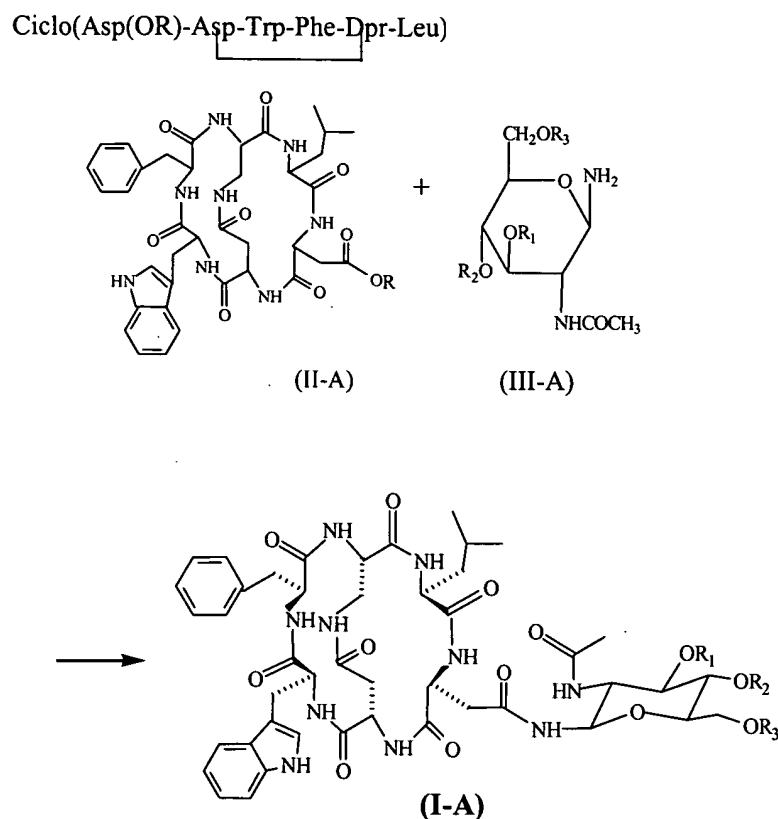
wherein  $R_1$ ,  $R_2$  and  $R_3$ , equal or different from each other, can be hydrogen or an oxygen protecting group, comprising the following steps:

1A) activation of the bicyclic peptide compounds of formula (I) with a suitable coupling agent to obtain a derivative of formula (II-A)



wherein R is a group selected from benzotriazole, possibly substituted with a halogen, azabenzotriazole and succinimidyl;

2A) reaction of the compound of formula (II-A) deriving from step 1A) in the presence of a solvent with the glycosidic derivative of formula (III-A)



wherein R, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> are defined as above.

10. (Currently amended) The process ~~Process~~ according to claim 9, wherein the compounds of formula (I-A) wherein R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are different from H, are transformed into the corresponding compounds of formula (I-A) wherein R<sub>1</sub>=R<sub>2</sub>=R<sub>3</sub>=H, by a deprotection reaction in the presence of a solvent.

11. (Currently amended) The process ~~Process~~ according to claim 9, wherein said oxygen protecting groups are selected from the group consisting of -COR<sub>4</sub> wherein R<sub>4</sub> is a linear or branched C1-C4 alkyl group, phenyl possibly substituted with a halogen atom, benzyl or benzoyl.

12. (Currently amended) The process ~~Process~~ according to claim 11, wherein said C1-C4 alkyl group is selected from the group consisting of methyl, ethyl, propyl, butyl, isopropyl and t-butyl.



13. (Currently amended) The process ~~Process~~ according to claim 12, wherein said C1-C4 alkyl group is methyl.

14. (Currently amended) The process ~~Process~~ according to claim 9, wherein said glycosidic derivatives of formula (III-A) are selected from the group consisting of 2-acetamide-2-deoxy- $\beta$ -D-glucopyranosylamine and 2-acetamide-3,4,6-tri-O-acetyl-2-deoxy- $\beta$ -D-glucopyranosylamine.

15. (Currently amended) The process ~~Process~~ according to claim 9, wherein said bicyclic peptide compounds of formula (I) are prepared as described in claim 1.

16. (Currently amended) The process ~~Process~~ according to claim 1, wherein said coupling agent is selected from the group consisting of isobutyl chloroformate, a carbodiimide possibly in combination with a hydroxy derivative, phosphonium salts, N-oxide guanidine salts and uronium salts.

17. (Currently amended) The process ~~Process~~ according to claim 9, wherein said coupling agent is selected from the group consisting of isobutyl chloroformate, a carbodiimide possibly in combination with a hydroxy derivative, phosphonium salts, N-oxide guanidine salts and uronium salts.

18. (Currently amended) The process ~~Process~~ according to claim 16, wherein said carbodiimides are selected from dicyclohexylcarbodiimide and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride; said hydroxy derivative is selected from 1-hydroxybenzotriazole, 6-chloro-1-hydroxybenzotriazole, hydroxysuccinimide and 1-hydroxy-7-azabenzotriazole; said phosphonium salts, N-oxide guanidine salts and uronium salts are selected from (Benzotriazol-1-yloxy)tri(dimethylamino)phosphonium hexafluorophosphate, (Benzotriazol-1-yloxy)tripyrrolidine phosphonium hexafluorophosphate, 1-[bis(dimethylamino)methylene]-1H-benzotriazolium-3-oxide hexafluorophosphate, 1-[bis(dimethylamino)methylene]-5-chloro-1H-benzotriazolium-3-oxide hexafluorophosphate, 1-[bis(dimethylamino)methylene]-1H-benzotriazolium-3-oxide tetrafluoroborate, 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazole[4,5-

b]pyridinium-3-oxide hexafluorophosphate, 1-[bis(dimethylamino)methylene]-5-chloro-1H-benzotriazolium-3-oxide tetrafluoroborate, O-[(ethoxycarbonyl)cyanomethylenamino]-N,N,N',N'-tetramethyluronium tetrafluoroborate, O-(bicyclo[2.2.1]hept-5-ene-2,3-dicarboximido)-N,N,N',N'-tetramethyluronium tetrafluoroborate, and O-(N-succinimidyl)-N,N,N',N'-tetramethyluronium tetrafluoroborate.

19. (Currently amended) The process ~~Process~~ according to claim 17, wherein said carbodiimides are selected from dicyclohexylcarbodiimide and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride; said hydroxy derivative is selected from 1-hydroxybenzotriazole, 6-chloro-1-hydroxybenzotriazole, hydroxysuccinimide and 1-hydroxy-7-azabenzotriazole; said phosphonium salts, N-oxide guanidine salts and uronium salts are selected from (Benzotriazol-1-yloxy)tri(dimethylamino)phosphonium hexafluorophosphate, (Benzotriazol-1-yloxy)tripyrrolidine phosphonium hexafluorophosphate, 1-[bis(dimethylamino)methylene]-1H-benzotriazolium-3-oxide hexafluorophosphate, 1-[bis(dimethylamino)methylene]-5-chloro-1H-benzotriazolium-3-oxide hexafluorophosphate, 1-[bis(dimethylamino)methylene]-1H-benzotriazolium-3-oxide tetrafluoroborate, 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazole[4,5-b]pyridinium-3-oxide hexafluorophosphate, 1-[bis(dimethylamino)methylene]-5-chloro-1H-benzotriazolium-3-oxide tetrafluoroborate, O-[(ethoxycarbonyl)cyanomethylenamino]-N,N,N',N'-tetramethyluronium tetrafluoroborate, O-(bicyclo[2.2.1]hept-5-ene-2,3-dicarboximido)-N,N,N',N'-tetramethyluronium tetrafluoroborate, and O-(N-succinimidyl)-N,N,N',N'-tetramethyluronium tetrafluoroborate.

20. (Currently amended) The process ~~Process~~ according to claim 1, wherein said coupling reactions are carried out in the presence of a tertiary amine in an organic solvent at a temperature comprised between -20 and +50°C.

21. (Currently amended) The process ~~Process~~ according to claim 9, wherein said coupling reactions are carried out in the presence of a tertiary amine in an organic solvent at a temperature comprised between -20 and +50°C.

22. (Currently amended) The process ~~Process~~ according to claim 20, wherein said tertiary amine is selected from the group consisting of N-methylmorpholine, triethylamine and diisopropylethylamine, and said organic solvent is selected from the group consisting of ethyl acetate, dimethylformamide and N-methylpyrrolidone.

23. (Currently amended) The process ~~Process~~ according to claim 21, wherein said tertiary amine is selected from the group consisting of N-methylmorpholine, triethylamine and diisopropylethylamine, and said organic solvent is selected from the group consisting of ethyl acetate, dimethylformamide and N-methylpyrrolidone.

24. (Currently amended) The process ~~Process~~ according to claim 1, wherein said deprotection reactions are carried out by means of hydrogenation in the presence of a catalyst in a solvent selected from solvents which dissolve the components of the reaction without reacting with them, excluding ketones and solvents which poison the catalyst, at a temperature comprised between -20 and +50°C.

25. (Currently amended) The process ~~Process~~ according to claim 10, wherein said deprotection reactions are carried out by means of hydrogenation in the presence of a catalyst in a solvent selected from solvents which dissolve the components of the reaction without reacting with them, excluding ketones and solvents which poison the catalyst, at a temperature comprised between -20 and +50°C.

26. (Currently amended) The process ~~Process~~ according to claim 24, wherein said catalyst is selected from 5% and 10% Palladium and said solvent is selected from dimethylformamide, N-methylpyrrolidone, acetic acid, p-toluenesulfonic acid, methanol, ethanol, isopropanol, and mixtures thereof.

27. (Currently amended) The process ~~Process~~ according to claim 25, wherein said catalyst is selected from 5% and 10% Palladium and said solvent is selected from dimethylformamide, N-methylpyrrolidone, acetic acid, p-toluenesulfonic acid, methanol, ethanol, isopropanol, and mixtures thereof.

28. (Currently amended) The process ~~Process~~ according to claim 1, wherein said deprotection reactions are carried out by means of acid treatment with pure acids or with acids mixed with other solvents, at a temperature comprised between -20 and +50°C.

29. (Currently amended) The process ~~Process~~ according to claim 10, wherein said deprotection reactions are carried out by means of acid treatment with pure acids or with acids mixed with other solvents, at a temperature comprised between -20 and +50°C.

30. (Currently amended) The process ~~Process~~ according to claim 28, wherein said acids are selected from hydrochloric acid, trifluoroacetic acid and formic acid.

31. (Currently amended) The process ~~Process~~ according to claim 29, wherein said acids are selected from hydrochloric acid, trifluoroacetic acid and formic acid.

32. (Currently amended) The process ~~Process~~ according to claim 1, wherein said deprotection reactions are carried out by means of treatment with a base compound in the presence of a solvent, at a temperature comprised between -20 and +50°C.

33. (Currently amended) The process ~~Process~~ according to claim 10, wherein said deprotection reactions are carried out by means of treatment with a base compound in the presence of a solvent, at a temperature comprised between -20 and +50°C.

34. (Currently amended) The process ~~Process~~ according to claim 32, wherein said base compound is selected from hydroxides of alkali metals or alkaline earth metals, and said solvent is selected from the group consisting of water, dioxane, acetonitrile, methanol, ethanol, isopropanol, and mixtures thereof.

35. (Currently amended) The process ~~Process~~ according to claim 33, wherein said base compound is selected from hydroxides of alkali metals or alkaline earth metals,

and said solvent is selected from the group consisting of water, dioxane, acetonitrile, methanol, ethanol, isopropanol, and mixtures thereof.